

REMARKS

Claim 7 has been cancelled. Claims 1 and 8 have been amended. Claims 1-6 and 8-9 are now pending in this application. Support for the amendments is found in the existing claims and the specification as discussed below. Accordingly, the amendments do not constitute the addition of new matter. Applicant respectfully requests the entry of the amendments and reconsideration of the application in view of the amendments and the following remarks.

Priority

The Office Action states that foreign priority to JP 2003-082739 has not been granted because an English translation of the document has not been provided. Applicants note that this contradicts the acknowledgement of the claim for foreign priority in the Office Action Summary.

In any case, an English translation of a priority document is not necessary to claim priority, but only to overcome an intervening reference (see M.P.E.P. 201.15). As no intervening reference has been cited, it is not necessary for Applicants to provide an English translation of a priority document.

Applicants assert that the priority claim has been properly made by listing of JP 2003-082739 on the Declaration/Power of Attorney document which was filed on November 7, 2005 and by submission of a certified copy of the foreign application (see M.P.E.P. 201.14(b)). As this application is the US National phase under 35 U.S.C. § 371, a copy of the certified priority document is conveyed by the International Bureau (PCT Rule 17.2(a)).

Applicants respectfully request acknowledgement of the priority claim.

Rejection under 35 U.S.C. § 112, second paragraph

Claim 1 is rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rejected as the acronym “ccm” is not clear. Claim 1 has been amended to replace “ccm” with the unabbreviated term “cytochrome c maturation”.

Claim 1 is also rejected on the basis that the term “in an expressible form” is not clear. Applicants respectfully submit that it would be clear to one skilled in the art that Applicants intend that the α and β forms of glucose dehydrogenase are linked to appropriate control segments, such as a promoter, so that the subunits are expressed in the bacterium.

Regarding Claims 1 and 3, Applicants respectfully submit that the definite article “the” is proper as the reference is specifically to the α -, β -, and γ - of the glucose dehydrogenase of *Burkholderia cepacia*. Reconsideration is requested.

In view of Applicants’ amendments and arguments, reconsideration and withdrawal of the above ground of rejection is respectfully requested.

Rejection under 35 U.S.C. § 102(b)

Claims 1-6 are rejected under 35 U.S.C. § 102 (b) as being anticipated by Sode (WO/2002/36779).

This ground of rejection is addressed by Applicants’ amendment to recite “...glucose dehydrogenase of *Burkholderia cepacia* in an expressible form and further comprising genes of a ccm operon operably linked to a promoter, thereby enhancing the expression of a cytochrome c maturation (ccm) system.” Support for the amendment is found in cancelled claim 7.

Sode does not teach this limitation. Accordingly, the claims as amended are not anticipated by Sode.

In view of Applicants’ amendments, reconsideration and withdrawal of the above ground of rejection is respectfully requested.

Rejection under 35 U.S.C. § 103(a)

Claims 1-9 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Sode (WO/2002/36779) in view of Herbaud, et al. (*Biochim. Biophys. Acta* vol. 1482(1): 18-24 (2000)) as evidenced by Arslan, et al. (*Biochem. Biophys. Res. Commun.* 251: 744-747 (1998)).

Sode only discloses expressing the α -subunit of glucose dehydrogenase (GDH). Although Sode discloses the partial 5’terminal sequence of the nucleotide sequence encoding the β -subunit of GDH and the N-terminal amino acid sequence thereof, Sode does not disclose the complete sequence of the β -subunit. Therefore, even if Sode is combined with the disclosures of Herbaud, et al. and Arslan, et al. on the ccm genes, one of ordinary skill in the art could not have achieved the present invention, because the β -subunit of GDH is not taught by any of the cited references. Accordingly, the cited references taken as a whole do not teach all of the claim elements.

Furthermore, even if there was an apparent reason to co-express the DNA encoding the β -subunit of GDH with the DNA encoding the α -subunit of GDH along with the ccm genes of

Herbaud, et al. or Arslan, et al. (which Applicants maintain there was no apparent reason to do based upon the cited references), it was not predictable that an enzyme complex having the α -subunit and the β -subunit would be produced recombinantly and have enzyme activity. Both Herbaud, et al. and Arslan, et al. teach co-expression of a cytochrome c with the ccm genes in an *E. coli*. On the other hand, Applicants' claimed invention is directed to "...DNAs encoding the α -subunit and the β -subunit of glucose dehydrogenase of *Burkholderia cepacia* in an expressible form and further comprising genes of a ccm operon operably linked to a promoter,...". That is, Applicants' claimed invention is directed to expression of the ccm genes along with a heterodimer, not cytochrome c, per se, as taught by Herbaud, et al. and Arslan, et al. Neither Herbaud, et al. nor Arslan, et al teach expression of the ccm genes with a heterodimer. Both references merely teach co-expression of the ccm genes with various cytochrome c's. There was no reasonable expectation of success that a heterodimer including a cytochrome c unit could be successfully coexpressed with the ccm genes based upon Herbaud, et al. and Arslan, et al. who only teach cytochrome c.

Furthermore, by co-expressing the enzyme complex including the γ -subunit, the α -subunit and the β -subunit with the ccm genes, the GDH activity in *Escherichia* bacterium increased to a level that was unexpected (present specification, page 20, second and third full paragraphs) compared to expressing the enzyme complex only and the wild type strain. While the activity of the recombinant *E. coli* which also included the genes for the ccm operon (JM109/pTRC99A $\gamma\alpha\beta$, pBBJMccm) was 32 U/mL, the two controls had activities of only 0.3 (JM109/pTRC99A $\gamma\alpha\beta$) and 1.4 (*Burkholderia cepacia* KS1). Such high expression levels could not have been predicted from the cited references. This result is not expected in view of Herbaud, et al. and Arslan, et al. which teach production of cytochrome c by co-expressing the ccm genes. By following the teaching of the present specification, the enzyme complex of GDH comprising cytochrome c is produced in large amounts by co-expressing the ccm genes. Thus, the present invention has unexpected effects in view of the cited references.

Applicants respectfully submit that Claims 2-9 are also patentable over Sode, Herbaud, et al. and Arslan, et al. at least for the reasons given above for claim 1 as claims 2-9 include all of the limitations of claim 1, which is patentable for the reasons given above. In particular, none of the cited references teach or suggest the γ -subunit as recited in claims 3 & 4.

In view of Applicants' amendments and arguments, reconsideration and withdrawal of this ground of rejection is respectfully requested.

No Disclaimers or Disavowals

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, the Applicants are not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. The Applicants reserve the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that the Applicants have made any disclaimers or disavowals of any subject matter supported by the present application.

Co-Pending Applications of Assignee

Applicant wishes to draw to the Examiner's attention to the following co-pending applications of the present application's assignee.

Serial Number	Title	Filed
11/665296	MUTANT GLUCOSE DEHYDROGENASE	13-Apr-2007
11/587333	MUTANT GLUCOSE DEHYDROGENASE	19-Oct-2006

CONCLUSION

In view of Applicants' amendments to the claims and the foregoing Remarks, it is respectfully submitted that the present application is in condition for allowance. Should the Examiner have any remaining concerns which might prevent the prompt allowance of the application, the Examiner is respectfully invited to contact the undersigned at the telephone number appearing below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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